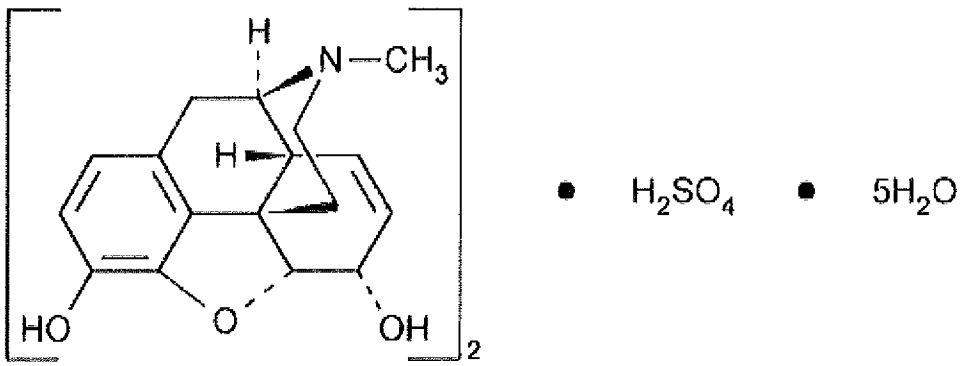
Morphine Sulfate

(mor' feen sul' fate).



USP Image 3D Image

$(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O$ 758.83

Morphinan-3,6-diol, 7,8-didehydro-4,5-epoxy-17-methyl, (5α,6α)-, sulfate (2:1) (salt), pentahydrate.

7,8-Didehydro-4,5α-epoxy-17-methylmorphinan-3,6α-diol sulfate (2:1) (salt) pentahydrate [6211-15-0].

Anhydrous 668.77 [64-31-3].

» Morphine Sulfate contains not less than 98.0 percent and not more than 102.0 percent of $(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4$, calculated on the anhydrous basis.

Packaging and storage— Preserve in tight, light-resistant containers. Store up to 40° as permitted by the manufacturer.

USP REFERENCE STANDARDS ⟨ 11 ⟩—

USP Morphine Sulfate RS

Identification—

A: *Infrared Absorption* ⟨ 197K ⟩: dried at 145° for 1 hour.

B: To 1 mg in a porcelain crucible or small dish add 0.5 mL of sulfuric acid containing, in each mL, 1 drop of *formaldehyde TS*: an intense purple color is produced at once, and quickly changes to deep blue-violet *(distinction from codeine, which gives at once an intense violet-blue color, and from hydromorphone, which gives at first a yellow to brown color, changing to pink and then to purplish red).*

C: To a solution of 5 mg in 5 mL of sulfuric acid in a test tube add 1 drop of *ferric chloride TS*, mix, and heat in boiling water for 2 minutes: a blue color is produced, and when 1 drop of

nitric acid is added, it changes to dark red-brown *(codeine and ethylmorphine give the same color reactions, but hydromorphone and papaverine do not produce this color change).*

D: A solution (1 in 50) responds to the tests for *Sulfate* ⟨ 191 ⟩.

SPECIFIC ROTATION ⟨ 781S ⟩: between −107° and −109.5°.

Test solution: the equivalent of 20 mg per mL, in water.

Acidity— Dissolve 500 mg in 15 mL of water, add 1 drop of *methyl red TS*, and titrate with 0.020 N sodium hydroxide: not more than 0.50 mL is required to produce a yellow color.

WATER, *Method I* ⟨ 921 ⟩: between 10.4% and 13.4% is found.

RESIDUE ON IGNITION ⟨ 281 ⟩: not more than 0.1%, from 500 mg.

Chloride— To 10 mL of a solution (1 in 100) add 1 mL of 2 N nitric acid and 1 mL of *silver nitrate TS*: no precipitate or turbidity is produced immediately.

Ammonium salts— Heat 200 mg with 5 mL of 1 N sodium hydroxide on a steam bath for 1 minute: no odor of ammonia is perceptible.

Limit of foreign alkaloids— Dissolve 1.00 g in 10 mL of 1 N sodium hydroxide in a separator, and shake the solution with three successive portions of 15, 10, and 10 mL of chloroform, passing the chloroform solutions through a small filter previously moistened with chloroform. Shake the combined chloroform solutions with 5 mL of water, separate the chloroform layer, and carefully evaporate on a steam bath to dryness. To the residue add 10.0 mL of 0.020 N sulfuric acid, and heat gently until dissolved. Cool, add 2 drops of *methyl red TS*, and titrate the excess acid with 0.020 N sodium hydroxide: not less than 7.5 mL is required (1.5%).

Assay—

Mobile phase— Dissolve 0.73 g of sodium 1-heptanesulfonate in 720 mL of water, add 280 mL of methanol and 10 mL of glacial acetic acid, mix, filter, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨ 621 ⟩).

Standard preparation— Dissolve an accurately weighed quantity of USP Morphine Sulfate RS in *Mobile phase,* and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 0.24 mg per mL. Prepare a fresh solution daily.

System suitability preparation— Dissolve suitable quantities of USP Morphine Sulfate RS and phenol in *Mobile phase* to obtain a solution containing about 0.24 and 0.15 mg per mL, respectively.

Assay preparation— Transfer about 24 mg of Morphine Sulfate, accurately weighed, to a 100-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see **CHROMATOGRAPHY** ⟨ 621 ⟩)— The liquid chromatograph is equipped with a 284-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation* and the *System suitability preparation,* and record the peak responses as directed for *Procedure:* the relative retention times are about 0.7 for phenol and 1.0 for morphine sulfate; the resolution, *R,* between phenol and morphine sulfate is not less than 2.0; the tailing factor for the morphine sulfate peak is not more than 2.0; and the relative standard deviation for replicate injections of the *Standard preparation* is not more than 2.0%.

Procedure— Separately inject equal volumes (about 25 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of $(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4$ in the portion of Morphine Sulfate taken by the formula:

$$100C(r_U / r_S)$$

in which C is the concentration, in mg per mL, of anhydrous morphine sulfate in the *Standard preparation,* as determined from the concentration of USP Morphine Sulfate RS corrected for moisture content by a titrimetric water determination; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Auxiliary Information— Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
Monograph	Clydewyn M. Anthony, Ph.D. Senior Scientific Liaison 1-301-816-8139	(SM22010) Monographs - Small Molecules 2
Reference Standards	RS Technical Services 1-301-816-8129 rstech@usp.org	

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Chromatographic Column—

MORPHINE SULFATE

Chromatographic columns text is not derived from, and not part of, USP 34 or NF 29.

Morphine Sulfate Extended-Release Capsules

DEFINITION

Morphine Sulfate Extended-Release Capsules contain NLT 90.0% and NMT 110.0% of the labeled amount of morphine sulfate pentahydrate $[(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O]$.

IDENTIFICATION

- **A. INFRARED ABSORPTION** ⟨197K⟩
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

- **PROCEDURE**

Diluent: Water. Adjust with phosphoric acid to a pH of 3.6.

Buffer solution: 13.8 mg/mL of monobasic sodium phosphate

Solution A: Acetonitrile, triethylamine, *Buffer solution*, and water (25:0.5:100:874.5). Adjust with phosphoric acid to a pH of 3.6.

Solution B: Acetonitrile

Mobile phase: See the gradient table below.

Time (min)	Solution A (%)	Solution B (%)
0	100	0
33	100	0
44	85	15
54	85	15
55	100	0
65	100	0

System suitability solution: 400 µg/mL of USP Morphine Sulfate RS and 10 µg/mL of USP Morphine Related Compound A RS and 10 µg/mL of USP Morphine Related Compound B RS (pseudomorphine) in *Diluent*

Standard solution: 1.0 mg/mL of USP Morphine Sulfate RS in *Diluent*

Sample stock solution: Transfer a weighed portion of the contents from NLT 20 Capsules, equivalent to 250 mg of morphine sulfate, to a 100-mL volumetric flask. Add 5 mL of methanol, and mix well for 30 min with gentle swirling every 5 min. Add *Diluent* up to half of the flask volume, and sonicate for 5 min to dissolve. Dilute with *Diluent* to volume.

Sample solution: 1.0 mg/mL of morphine sulfate from *Sample stock solution* in *Diluent*.

Pass through a suitable filter, and use the clear filtrate.

Chromatographic system

(See *Chromatography* 〈 621 〉, *System Suitability*.)

Mode: LC

Detector: UV 245 nm

Guard column: Packing L1

Column: 3.9-mm × 30-cm; 10-µm packing L1

Flow rate: 2 mL/min

Injection size: 40 µL

System suitability

Samples: *System suitability solution* and *Standard solution*

Suitability requirements

Resolution: NLT 2.0 between the morphine related compound A and morphine sulfate peaks, *System suitability solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Standard solution* and *Sample solution*

Calculate the percentage of $(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O$ in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = peak response from the *Sample solution*

r_S = peak response from the *Standard solution*

C_S = concentration of USP Morphine Sulfate RS in the *Standard solution* (mg/mL)

C_U = nominal concentration of the *Sample solution* (mg/mL)

Acceptance criteria: 90.0%–110.0%

PERFORMANCE TESTS

- **DISSOLUTION** 〈 711 〉

pH 7.5 phosphate buffer: 6.8 mg/mL of monobasic potassium phosphate and 1.6 mg/mL of sodium hydroxide. Adjust with phosphoric acid or 2 N sodium hydroxide to a pH of 7.5.

Medium: Proceed as directed for *Procedure* for *Method B* under *Apparatus 1 and Apparatus 2, Delayed-Release Dosage Forms*, observing the following exceptions. Perform *Acid Stage* testing, using 500 mL of 0.1 N hydrochloric acid for 1 h; and perform *Buffer Stage* testing, using 500 mL of *pH 7.5 phosphate buffer* for NLT 8 h.

Apparatus 1: 100 rpm

Times: 1, 4, 6, and 9 h

Determine the amount of $(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O$ dissolved by using the following method.

Mobile phase: Methanol, glacial acetic acid, and water (28:1:72), containing 0.73 g of sodium 1-heptanesulfonate

System suitability solution: 0.1 mg/mL each of phenol and USP Morphine Sulfate RS in *Mobile phase*

Standard solution: USP Morphine Sulfate RS in *pH 7.5 phosphate buffer* to obtain a solution having a known concentration corresponding to that of the *Sample solution*

Sample solution: Sample per *Dissolution* ⟨ 711 ⟩.

Chromatographic system

(See *Chromatography* ⟨ 621 ⟩, *System Suitability*.)

Mode: LC

Detector: UV 284 nm

Column: 3.9-mm × 30-cm; 10-µm packing L1

Flow rate: 2 mL/min

Injection size: 25 µL

System suitability

Sample: *System suitability solution*

[NOTE—The relative retention times for phenol and morphine sulfate are about 0.8 and 1.0, respectively.]

Suitability requirements

Resolution: NLT 2.0 between the phenol and morphine sulfate peaks

Tailing factor: NMT 2.0 for the morphine sulfate peak

Relative standard deviation: NMT 2.0%

Analysis

Samples: *Standard solution* and *Sample solution*

Tolerances: The percentage of the labeled amount of $(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O$ dissolved in 1 h conforms to *Dissolution* ⟨ 711 ⟩, *Extended-Release Dosage Forms, Acceptance Table 3*. The percentages of the labeled amount of $(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O$ dissolved at the other times specified conform to *Dissolution* ⟨ 711 ⟩, *Extended-Release Dosage Forms, Acceptance Table 2*.

Time (h)	Amount Dissolved
1	NMT 10%
4	25%–50%

6	50%–90%
9	NLT 85%

- **UNIFORMITY OF DOSAGE UNITS** ⟨ 905 ⟩ : Meet the requirements

IMPURITIES

Organic Impurities

- **PROCEDURE**

Diluent, Solution A, System suitability solution, Standard solution, Chromatographic system, and **Sample solution:** Proceed as directed in the *Assay.*

Sensitivity solution: 0.5 µg/mL of USP Morphine Sulfate RS in *Diluent*

System suitability

Samples: *System suitability solution*, *Standard solution*, and *Sensitivity solution*

Suitability requirements

Resolution: NLT 2.0 between the morphine related compound A and morphine sulfate peaks, *System suitability solution*

Sensitivity: Morphine peak is detectable, *Sensitivity solution*

Relative standard deviation: NMT 2.0%, *Standard solution*

Analysis

Samples: *Diluent* and *Sample solution* [NOTE—Disregard the peaks corresponding to those obtained in the chromatogram of the *Diluent.*]

Calculate the percentage of each impurity in the portion of Capsules taken:

$$\text{Result} = (r_U/r_S) \times (1/F) \times 100$$

r_U = peak response for each impurity from the *Sample solution*

r_S = peak response for morphine sulfate from the *Standard solution*

F = relative response factor from *Impurity Table 1*

Acceptance criteria

Any individual impurity: See *Impurity Table 1.*

Total impurities: NMT 1.5%

Impurity Table 1

Name	Relative Retention Time	Relative Response Factor	Acceptance Criteria, NMT (%)
Morphine related compound A[a]	1.4	1.0	0.5
Morphine sulphate	1.0	—	—

Morphine related compound B[b]	2.3	2.1	0.5
Any unspecified impurity	—	—	0.2

[a] 7,8-Didehydro-4,5α-epoxy-17-methylmorphinan-3,6α-diol, *N*-oxide.

[b] 2,2'-Bimorphine.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers, and store at controlled room temperature.
- **USP REFERENCE STANDARDS** ⟨ 11 ⟩

  USP Morphine Sulfate RS

  USP Morphine Related Compound A RS

  7,8-Didehydro-4,5α-epoxy-17-methylmorphinan-3,6α-diol, *N*-oxide.

  $C_{17}H_{19}NO_4$

  301.34

  USP Morphine Related Compound B RS

  2,2′-Bimorphine.

  $C_{34}H_{36}N_2O_6$

  568.66

Auxiliary Information— Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
Monograph	Clydewyn M. Anthony, Ph.D. Senior Scientific Liaison 1-301-816-8139	(SM22010) Monographs - Small Molecules 2
⟨ 711 ⟩	Margareth R.C. Marques, Ph.D. Senior Scientific Liaison 1-301-816-8106	(GCDF2010) General Chapters - Dosage Forms
Reference Standards	RS Technical Services 1-301-816-8129 rstech@usp.org	

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Morphine Sulfate Injection

» Morphine Sulfate Injection is a sterile solution of Morphine Sulfate in Water for Injection. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of morphine sulfate pentahydrate $[(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O]$. Injection intended for intramuscular or intravenous administration may contain sodium chloride as a tonicity-adjusting agent, and suitable antioxidants and antimicrobial agents. Injection intended for intrathecal or epidural use may contain sodium chloride as a tonicity-adjusting agent, but contains no other added substances.

Packaging and storage— Preserve in single-dose or in multiple-dose containers, preferably of Type I glass, protected from light. Preserve Injection labeled "Preservative-free" in single-dose containers.

Labeling— It meets the requirements for *Labeling* under *Injections* ⟨ 1 ⟩. Label it also to state that the Injection is not to be used if its color is darker than pale yellow, if it is discolored in any other way, or if it contains a precipitate. Injection containing no antioxidant or antimicrobial agents prominently bears on its label the words "Preservative-free," and includes, in its labeling, its routes of administration and the statement that it is not to be heat-sterilized. Injection containing antioxidant or antimicrobial agents includes in its labeling its routes of administration and the statement that it is not for intrathecal or epidural use.

USP REFERENCE STANDARDS ⟨ 11 ⟩ —

USP Endotoxin RS

USP Morphine Sulfate RS

Identification—

A: Dilute with methanol, if necessary, a volume of Injection to obtain a solution containing 500 µg per mL. Apply 20 µL of this solution and 20 µL of a solution of USP Morphine Sulfate RS in a mixture of methanol and water (1:1) containing 500 µg per mL to a suitable thin-layer chromatographic plate (see *Chromatography* ⟨ 621 ⟩) coated with a 250-µm layer of chromatographic silica gel mixture. Allow the spots to dry, and develop the chromatogram in a solvent system consisting of a mixture of acetone, methanol, and ammonium hydroxide (50:50:1) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the developing chamber, mark the solvent front, and allow the solvent to evaporate. Locate the spots on the plate by examination under short-wavelength UV light: the R_F value of the principal spot obtained from the Injection corresponds to that obtained

from the Standard solution.

B: It responds to the barium chloride test for *Sulfate* ⟨ 191 ⟩.

BACTERIAL ENDOTOXINS ⟨ 85 ⟩— It contains not more than 17.0 USP Endotoxin Units per mg of morphine sulfate; if labeled for intrathecal use, it contains not more than 14.29 USP Endotoxin Units per mg of morphine sulfate.

PH ⟨ 791 ⟩: between 2.5 and 6.5.

PARTICULATE MATTER ⟨ 788 ⟩— meets the requirements under small-volume Injections.

Other requirements— It meets the requirements under *Injections* ⟨ 1 ⟩.

Assay—

Mobile phase , *Standard preparation*, *System suitability preparation*, and *Chromatographic system*—Prepare as directed in the *Assay* under *Morphine Sulfate*.

Assay preparation— Transfer an accurately measured volume of Injection, equivalent to about 24 mg of morphine sulfate, to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Procedure— Proceed as directed for *Procedure* in the *Assay* under *Morphine Sulfate*. Calculate the quantity, in mg, of morphine sulfate pentahydrate $[(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O]$ in each mL of the Injection taken by the formula:

$$(758.85 / 668.77)(100C / V)(r_U / r_S)$$

in which 758.85 and 668.77 are the molecular weights of morphine sulfate pentahydrate and anhydrous morphine sulfate, respectively, V is the volume, in mL, of Injection taken, and the other terms are as defined therein.

Auxiliary Information— Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
Monograph	Clydewyn M. Anthony, Ph.D. Senior Scientific Liaison 1-301-816-8139	(SM22010) Monographs - Small Molecules 2
Reference Standards	RS Technical Services 1-301-816-8129 rstech@usp.org	
⟨ 85 ⟩	Radhakrishna S Tirumalai, Ph.D. Principal Scientific Liaison 1-301-816-8339	(GCM2010) General Chapters - Microbiology

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Chromatographic Column—

MORPHINE SULFATE INJECTION

Chromatographic columns text is not derived from, and not part of, USP 34 or NF 29.

Morphine Sulfate Suppositories

» Morphine Sulfate Suppositories contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of morphine sulfate pentahydrate $[(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O]$.

SUPPOSITORIES COMPOUNDED IN FATTY ACID BASE

Prepare Morphine Sulfate Suppositories in Fatty Acid Base as follows (see *Pharmaceutical Compounding—Nonsterile Preparations* 〈795〉):

Morphine Sulfate	50 mg
Silica Gel	25 mg
Fatty Acid Base, a sufficient quantity to make one suppository	

Calibrate the actual molds with the Fatty Acid Base that is used for preparing the Suppositories, and adjust the formula accordingly. Mix thoroughly the Morphine Sulfate and Silica Gel to obtain a uniform powder. Heat the Fatty Acid Base slowly and evenly until melted. Slowly add the powder to the melted base, with stirring. Mix thoroughly, and pour into molds. Cool, trim, and wrap.

Packaging and storage— Preserve in tight containers, and store in a refrigerator.

Labeling— Label Suppositories to state that they are Morphine Sulfate Suppositories in a Fatty Acid Base and to state that they are for rectal use only. Label Suppositories to state that they are to be stored in a refrigerator (2° to 8°). The label also bears a warning that the Suppositories are a specially formulated strength to be used only by the patient for whom they were prescribed, and that wrappers are to be removed prior to use.

USP REFERENCE STANDARDS 〈11〉—

USP Morphine Sulfate RS

UNIFORMITY OF DOSAGE UNITS 〈905〉: meet the requirements for *Weight Variation*.

Beyond-use date— Ninety days after the day on which they were compounded.

Compliance assay for suppositories compounded in fatty acid base—

Mobile phase— Dissolve 5.5 g of sodium 1-heptanesulfonate in 700 mL of water. Add 300 mL of methanol and 10 mL of glacial acetic acid, mix, filter, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* 〈621〉).

Standard preparation— Dissolve an accurately weighed quantity of USP Morphine Sulfate RS in *Mobile phase*, and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution having a known concentration of about 0.5 mg per mL. [NOTE—Prepare this

solution fresh daily.]

System suitability preparation— Prepare a solution in *Mobile phase* containing, in each mL, about 0.24 mg of USP Morphine Sulfate RS and 0.15 mg of phenol.

Assay preparation— Transfer 1 Suppository to a 60-mL separator containing 20 mL of chloroform and 20 mL of 0.01 N hydrochloric acid, and shake to dissolve the Suppository. Transfer the chloroform layer to a 250-mL separator. Extract the aqueous layer with a second 20-mL portion of chloroform, and combine the chloroform extracts in the 250-mL separator. Wash the chloroform extracts with two additional 20-mL portions of 0.01 N hydrochloric acid, combine the aqueous layers in a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix. Pass this solution through a filter having a 0.45-µm or finer porosity, discarding the first 4 mL of the filtrate.

Chromatographic system (see **CHROMATOGRAPHY** ⟨ 621 ⟩)— The liquid chromatograph is equipped with a 284-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The column temperature is maintained at 30°. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation* and the *System suitability preparation*, and record the peak responses as directed for *Procedure:* the relative retention times are about 0.7 for phenol and 1.0 for morphine; the resolution, *R*, between phenol and morphine is not less than 2.0; the tailing factor for the morphine peak is not more than 2.0; and the relative standard deviation for replicate injections of the *Standard preparation* is not more than 2.0%.

Procedure— Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of morphine sulfate pentahydrate $[(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O]$ in the Suppository taken by the formula:

$$(758.83/668.77)(100C)(r_U / r_S)$$

in which 758.83 and 668.77 are the molecular weights of morphine sulfate pentahydrate and anhydrous morphine sulfate, respectively; *C* is the concentration, in mg per mL, of anhydrous morphine sulfate in the *Standard preparation*, as determined from the concentration of USP Morphine Sulfate RS corrected for moisture content by a titrimetric water determination; and r_U and r_S are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

SUPPOSITORIES COMPOUNDED IN POLYETHYLENE GLYCOL BASE

Prepare Morphine Sulfate Suppositories in Polyethylene Glycol Base as follows (see *Pharmaceutical Compounding—Nonsterile Preparations* ⟨ 795 ⟩):

Morphine Sulfate	50 mg

Silica Gel	25 mg
Polyethylene Glycol Base, a sufficient quantity to make one suppository	

Calibrate the actual molds with Polyethylene Glycol Base that is used for preparing the Suppositories, and adjust the formula accordingly. Mix thoroughly the Morphine Sulfate and Silica Gel to obtain a uniform powder. Heat the Polyethylene Glycol Base slowly and evenly until melted. Slowly add the powder to the melted base, with stirring. Mix thoroughly, and pour into molds. Cool, trim, and wrap.

Packaging and storage— Preserve in tight containers, and store in a refrigerator. Do not dispense or store polyethylene glycol–base suppositories in polystyrene containers.

Labeling— Label Suppositories to state that they are Morphine Sulfate Suppositories in a Polyethylene Glycol Base and to state that they are for rectal use only. Label Suppositories to state that they are to be stored in a refrigerator (2° to 8°). The label also bears a warning that the Suppositories are a specially formulated strength to be used only by the patient for whom they were prescribed, and that wrappers are to be removed prior to use.

USP REFERENCE STANDARDS ⟨ 11 ⟩ —

USP Morphine Sulfate RS

UNIFORMITY OF DOSAGE UNITS ⟨ 905 ⟩: meet the requirements for *Weight Variation.*

Beyond-use date— Ninety days after the day on which they were compounded.

Compliance assay for suppositories compounded in polyethylene glycol base—

Mobile phase, *Standard preparation*, *System suitability preparation*, and *Chromatographic system*— Proceed as directed in the *Compliance assay for suppositories compounded in fatty acid base.*

Assay preparation— Transfer 1 Suppository to a 100-mL volumetric flask, and add about 70 mL of *Mobile phase.* Sonicate for 15 minutes to dissolve the Suppository, cool, dilute with *Mobile phase* to volume, and mix. Pass a 10-mL portion of the solution through a filter having a 0.45-µm or finer porosity, discarding the first 4 mL of the filtrate.

Procedure— Proceed as directed in the *Compliance assay for suppositories compounded in fatty acid base.* Calculate the quantity, in mg, of morphine sulfate pentahydrate $[(C_{17}H_{19}NO_3)_2 \cdot H_2SO_4 \cdot 5H_2O]$ in the Suppository taken by the formula:

$$(758.83/668.77)(100C)(r_U / r_S)$$

in which the terms are as defined therein.

Auxiliary Information— Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
Monograph	Rick G. Schnatz, Pharm.D. Scientific Liaison 1-301-816-8526	(CMP2010) Compounding
Reference Standards	RS Technical Services 1-301-816-8129 rstech@usp.org	

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Chromatographic Column—

MORPHINE SULFATE SUPPOSITORIES

Chromatographic columns text is not derived from, and not part of, USP 34 or NF 29.